Appendix C

Evaluations of Barrier Creams[1]

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IN VITRO DATA

In vitro studies test the effects of barrier creams on the skin, which mimics the reaction of *in vivo* skin. The *in vitro* method provides not only qualitative data (i.e., distinguishes between the creams) but also quantitative data (i.e., differences in absorption). Langford (1978) conducted *in vitro* studies to determine the behavior of a formulated fluorochemical-resin complex and a number of other solvents. He tested penetration through treated filter paper, repellency on treated pigskin, and penetration of radio-labeled sodium lauryl sulfate through treated hairless mouse skin. The fluorochemical-resin complex provided the best resistance against a range of solvents.

Reiner et al. (1982) studied the protective effect of model ointments on guinea pig skin *in vitro*. The permeation values of a toxic agent through unprotected and protected skin within 10 hours as a function of time were determined radiologically and enzymatically. Permeation of the toxic agent was markedly reduced by ointments with a polyethylene glycol base and ointments containing active substances.

Loden (1986) evaluated the effects of barrier creams on the absorption of (^{13}H)-water (^{14}C)-benzene and (^{14}C)-formaldehyde by excised human

[1]The following material was prepared for the use of the principal investigators of this study. The opinions and conclusions herein are the authors' and not necessarily those of the National Research Council.

skin. The control skins and treated skins were exposed to the test substance for 30 minutes, and the amount absorbed was determined. The model experimental "water barrier" cream reduced the absorption of water and benzene but not formaldehyde. Only one cream slightly reduced the absorption of benzene and formaldehyde; the others did not.

Fullerton and Menne (1995) tested the protective effect of ethylenediaminetetraacetate barrier gels against nickel contact allergy in *in vitro* and *in vivo* studies. In an *in vitro* study, about 30 mg of barrier gel was applied on the epidermal side of the skin and a nickel disc applied. After 24 hours, the disc was removed, the epidermis was separated from the dermis, and the nickel content in the epidermis and dermis was quantified by adsorption differential pulse voltammetry. The amount of nickel in the epidermal skin layer on treated skins was significantly less than the amount in untreated skins.

Zhai et al. (1999) used an *in vitro* diffusion system to measure the protective effect of quaternium-18 bentonite gels to prevent 1 percent concentration of [^{35}S] sodium lauryl sulfate penetration in human cadaver skin. The accumulated amount in receptor cell fluid was measured to evaluate the model gels over 24 hours. The test gels significantly decreased absorption when compared to the control samples of unprotected skin.

Treffel et al. (1994) measured the effectiveness on human skin of barrier creams against dyes (eosin, methylviolet, and oil red O) with varying n-octanol/water partition coefficients (0.19, 29.8 and 165, respectively). Barrier cream effects were assayed by measuring the dyes in the epidermis of protected skin samples after 30 minutes. They found no correlation between the galenic (pharmaceutic) parameters of the assayed products and the protection level, indicating that neither the water content nor the consistency of the formulations affected the level of protection. This physicochemical data could be used for tailoring barrier creams to meet the challenges of specific chemical agents.

IN VIVO DATA

Mahmoud and Lachapelle (1985) and Lachapelle et al. (1990) used a guinea pig model to evaluate the protective value of barrier creams and/or gels by laser Doppler flowmetry (blood flow) and histological assessment. The histopathological damage after 10 minutes of contact to toluene was mainly confined to the epidermis; the dermis was almost normal. Dermal blood flow changes were relatively high on the control site compared to the sites pretreated with gel. In addition, the blood concentrations of n-hexane in the control group and the gel-pretreated group were

determined. It was possible to correlate results found by invasive (blood levels) and noninvasive techniques.

Frosch et al. (1993a, 1993b, 1993c), and Frosch and Kurte (1994) developed the repetitive irritation test in the guinea pig and in humans to evaluate barrier creams using a series bioengineering techniques. The pretreated and untreated test skin (guinea pig or human) was exposed daily to the irritants for two weeks. The resulting irritation was scored on a visual scale and assessed by biophysical (bioengineering) techniques. Some test creams suppressed irritation with all test parameters; some showed no effect, and even increased irritation.

Zhai and Maibach (1996) used an *in vivo* human model to measure the effectiveness of barrier creams against dye indicator solutions, methylene blue in water and oil red 0 in ethanol, representative of model hydrophilic and lipophilic compounds. Solutions of 5 percent methylene blue and 5 percent oil red O were applied to untreated and barrier-cream pretreated skin with the aid of aluminum occlusive chambers, for either a few minutes or four hours. At the end of the application time, the materials were removed and consecutive skin surface biopsies were taken. The amount of dye that had penetrated into each strip was determined by colorimetry. Two model creams were effective; one increased the cumulative amount of dye.

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